higher scores for chronic inflammation compared to those with *dupA*-negative strains (2.36 vs. 2.24, p = 0.058). The presence of *dupA* was not associated with the *cagA*, *vacA*, *iceA* or *babA 2* genotypes.
Conclusions: In Shanghai the prevalence of *dupA* gene was highest in DU and inversely related to GU and gastric cancer both which are associated with corpus atrophy.

I-17 Antimicrobial susceptibility testing through EUCAST

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In order to categorise a bacterium as sensitive to an antibiotic, it is necessary to perform a phenotypic antimicrobial susceptibility test. Phenotypic AST systems need breakpoints to. categorise bacteria S, I or R. Breakpoints are best determined by breakpoint committees consisting of experts in the fields of clinical microbiology and infectious diseases. Both CLSI (formerly NCCLS in the USA) and EUCAST (the European Committee on Antimicrobial Susceptibility Testing) are well known breakpoint committees. The former is a commercial enterprise engaging the pharmaceutical industry and the profession whereas the EUCAST is organised by the European Centre for Disease Control, the European Medicines Evaluation Agency and the European Society for Clinical Microbiology and Infectious Diseases. EUCAST has harmonised breakpoints for Europe and acts as the EMEA breakpoint committee during the process of approval of new drugs.
EUCAST breakpoints are currently being introduced in automated systems for AST. The Phoenix from Becton Dickinson is already validated with EUCAST breakpoints and the Vitek2 from BioMerieux is to follow. A disk test based on Mueller Hinton agar and 108 cfu/mL inoculum is currently being developed by EUCAST.
New therapeutic traditions, dosage practices, new tools for setting breakpoints and most importantly new resistance mechanisms necessitates an evolutionary process for clinical breakpoints. EUCAST has an active process for reviewing and revising breakpoints.
EUCAST offers free documents on breakpoints, methods and interpretive criteria on its website (www.eucast.org) which also displays MIC- (and eventually zone diameter-) distributions of wild type bacteria on the website. These can be used for calibration of methods.

I-18 *Laribacter hongkongensis*: From discovery to complete genome sequence

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Despite extensive investigations, a microbiological cause cannot be found in about half of the patients with infectious disease. Throughout the years, scientists have spent tremendous efforts in looking for microorganisms associated with these "unexplained infectious disease syndromes". In 2001, we discovered *Laribacter hongkongensis* gen. nov. sp. nov., a facultative anaerobic, Gram-negative, S-shaped, urease-positive rod of the Neisseriaceae family, from blood and empyema thoracis of a patient with alcoholic cirrhosis. During the past seven years, we have documented that *L. hongkongensis* was associated with gastroenteritis and traveler's diarrhea and cases were found globally in patients who resided in or had recent travel histories to countries in Asia, Europe, America and Africa. We have found that freshwater fish is the reservoir and it was also found in drinking water reservoirs. We have cloned the beta-lactamase and tetracycline resistance genes and developed gene deletion and expression systems for *L. hongkongensis*. Due to the potential of its clinical importance and related ecology, important phenotypic characteristics and phylogenetic position, and the availability of genetic manipulation systems for downstream experiments, we sequenced the complete genome of *L. hongkongensis*, with the aim of achieving better understanding of its biology, mechanism of adaptation to different hosts, and virulence mechanisms.

I-19 Antibiotic resistance in gram-negative pathogens: Dealing with untreatable infections

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While resistant gram-positive pathogens such as MRSA and VRE have received a lot of attention especially in the US and Europe, there have been rising numbers of multi-resistant and even pan-drug resistant strains of gram-negative bacilli in particular Pseudomonas and Acinetobacter spp. These have posed tremendous challenges to the clinicians looking after patients especially in Asia and Southern Europe. With limited therapeutic options, a greater focus on prevention and control has resulted. We are also hampered by a lack of good data to explain the emergence of these pathogens and to understand the reasons for their spread to our vulnerable patients.

I-20 Two stage theory pathogenic mechanism of *Streptococcus suis*

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Streptococcus suis infections are enzootic in pigs where sporadic cases occur in humans. Since the first human case was recorded in 1968, only 250 cases have been reported globally through June 2005. The majority of the cases have resulted in meningitis often associated with hearing loss. During the period from July to August 2005, however, an explosive outbreak of 215 cases of human infection occurred in Sichuan Province, China. Sixty-one of the 215 (28%) patients presented an unusual streptococcal toxic shock like syndrome (STSLS) with high mortality (38 of 61; 62%) in previously healthy farmers. Both the clinical presentation and epidemiology features of the Sichuan outbreak had not previously been observed.
This outbreak was caused by a mutant *S. suis* named as sequence type 7 (ST7) using the multi-locus sequence typing method, the method of choice for addressing questions related to genotyping for epidemiological studies, population, and evolutionary biology. The ST7 strain caused a single case described from Hong Kong in 1996; then it emerged to cause a small outbreak in Jiangsu in 1998; and spread to cause the largest ever outbreak with severe shock in 2005.
It was found that the serum levels of IL-1β, IL-6, IL-8, IL-12, p70, IFN-γ and TNF-α, the inflammation cytokines, during the early phase of the disease were significantly elevated in patients with STSLS compared to those with meningitis only. And, the serum levels of pro-inflammatory cytokines were significantly higher in mice infected with the ST7 strain than in those infected with either the ST1 or ST25 strains.
Genome comparisons showed the ST1 strain had acquired 132 genomic islands, including 5 pathogenicity islands, and the "epidemic" strain ST7 had acquired an additional 5 genomic islands. Therefore, We proposed the intermediate virulent ST25 type evolved to become the highly pathogenic

ST1 type; and in-turn evolved recently to become the "epidemic" ST7 type. The virulence increased in the ST7 type with its ability to stimulate massive amounts of pro-inflammatory cytokines that led to the Streptococcal toxic shock like syndrome.
Based on the information generated, we proposed a two stage theory for the pathogenic mechanism of *S. suis*. When the pathogen enters the human body (bloodstream), stage one is initiated showing communication between bacterial cell wall components with the host immune system using pattern recognition receptors such as Toll-like receptor 2 and CD14; and probably by using the two-component signal transduction system acquired recently with the consequent burst of pro-inflammatory cytokines. The ST7 *S. suis* would have mutated to stimulate the host to produce massive amount of cytokines such as TNF-α, IL-1β and interferon gamma that regulate high production levels of other cytokines such as IL-6 and IL-12, leading to the STSLS. If a patient survives the first stage, the pathogen may reach the central nervous system traveling free in the circulation or monoctye-associated to cause the meningitis. The clinical significance of these findings was to prevent sudden death associated with ST7 or ST1 *S. suis* infections where the treatment was initiated early during the acute phase of the infection, specially for therapies to prevent or reduce the risk of STSLS.

Concurrent Session 3 – HIV – Overview

I-21 Prevalence of drug resistant HIV-1 in rural areas of Hubei province in the People's Republic of China

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Objective: To determine the prevalence of drug resistant HIV-1 and the efficacy of first-line HAART regimens consisting of generic NRTI and NNRTI among 339 study subjects in rural areas of Hubei province, China.
Methods: Two cross-sectional studies were conducted to investigate 150 HAART-naive (99 received subsequent therapy) between 2003 and 2005 and 288 HAART-experienced patients between 2006 and 2007. Patients' $CD4^+$ T-cell count and viral load were determined. HIV-1 *pol* gene fragments were amplified from patients' plasma by RT-PCR, subsequently sequenced and analyzed.
Results: 83.5% of the patients were from rural villages. They were dominantly infected with subtype B′ HIV-1 (97.4%) through paid blood donation (64.6%) and related blood transfusion (28.3%). We found that there was a steady increase of CD4 count over time among treated patients without detectable viral load (186/288, 64.6%). There was, however, an increasing prevalence of NRTI and NNRTI resistant mutations among patients with detected viremia (102/288, 35.4%) after treatment for 3–6 (24.3%), 9–12 (57.1%) and 20–24 (63.3%) months, respectively. The increasing rates were associated with significant CD4 count drop and viral load increase. Some patients also developed multi-drug resistant mutants.
Conclusions: We report the first HIV-1 drug resistance study after two-years on HAART among Chinese patients living in rural villages. Our data suggest that a significant portion of patients are failing first-line regimens with a trend of AIDS progression. It is therefore necessary to maximize the drug adherence and to make affordable second-line HAART regimens available immediately. Our results have implications for implementing HAART in under-resourced developing country settings.

I-22 Molecular epidemiology of drug resistant HIV-1 in Hong Kong

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The combination antiretroviral therapy is referred as Highly Active Antiretroviral Therapy (HAART) which inhibits different pathways of HIV pathogenesis so that viral replication can be effectively suppressed. Following the introduction of HAART since late 90s, significant decline in morbidity, mortality and HIV/AIDS incidence was reported in Hong Kong. To monitor the efficacy of HAART, genotyping resistance test (GRT) by PCR-sequencing of the viral *pol* gene (PR codon 1 to RT codon 410) was used to study 1,015 samples collected from 830 HIV-1+ patients. Results showed good concordance to clinical response among treatment experienced patients. Primary resistance was detected among 6.7% of the treatment naive samples and GRT also revealed the predominant subtypes CRF01_AE (45.8%) and B (41.2%) were followed by C (4.4%), CRF07_BC (1.7%), A1 (1.3%), CRF08_BC (0.9%), CRF02_AG (0.6%), CRF06_cpx (0.3%) and G (0.1%). Mutations D30N, G48V and I84V were only detected in subtype B while V32I mutation was only detected in CRF01_AE. Resistance associated with HAART were detected among 10% treatment experienced patients after 18–24 months on HAART in Hong Kong. Increasing prevalence of the primary resistance in Hong Kong was detected since 1997 without subtype preference. The presence of primary resistance in treatment naive patients indicates the need for GRT on pre- and post-treatment samples, so that appropriate regimens for HAART can be implemented. Phylogenetic analysis of the *pol* gene also identified 3 major local clusters of CRF01_AE subtypes and B subtypes which were clonally related to reference sequences from major cities in China (Fujian, Pingxiang and Nanning).

I-23 Opportunistic infections in AIDS: Thai experience

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The first Thai AIDS case was imported in 1984, since then approximately one million Thais have been infected with HIV, and currently, the estimated prevalence of HIV infection is about 1%. There were 5 consecutive epidemic waves as follows: among male homosexuals (started 1985), rapid surge in intravenous drug users (1988), followed by female commercial sex workers (1989), their male clients (1990) and lastly wives and newborn of the latter (1991). Most HIV infection is transmitted via heterosexual activities. This spreading of infection occurred rapidly and caused great alarm to all people involved.
Fortunately, the Thai Government at that time has recognized this problem and considered AIDS prevention and control a high national priority, involving several ministries: Education, Health, Interior, etc. Thailand has successfully slowed down the epidemic. However, hundred thousands of people have already been infected. Prior to the HAART era, hundreds of HIV-infected people became ill with opportunistic infections (OI) and hence the diagnosis of AIDS with high mortality. From our experience during